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PATENT COOPERATION TREA..

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 02 March 2000 (02.03.00)	
International application No. PCT/US99/12680	**Applicant's or agent's file reference** 22727/04039
International filing date (day/month/year) 04 June 1999 (04.06.99)	**Priority date** (day/month/year) 05 June 1998 (05.06.98)
Applicant BISARO, David	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

30 December 1999 (30.12.99)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer R. Forax
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 22727/04039	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/12680	International filing date *(day/month/year)* 04 JUNE 1999	Priority date *(day/month/year)* 05 JUNE 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant THE OHIO STATE RESEARCH FOUNDATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30 DECEMBER 1999	28 JULY 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ASHWIN MEHTA Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/12680

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-21, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the claims:
pages 22-24, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the drawings:
pages 1-5, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE
[X] the claims, Nos. NONE
[X] the drawings, sheets/~~fig~~ NONE

5. [X] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/12680

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 24

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 24 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/12680

IV. Lack of unity f invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s)1-6, 15, 16, 19, 21 and 22, drawn to a first product, an isolated single domain AL2 gene, and a first method for preparing a plant that is more susceptible to viral infection, comprising transforming a plant sample with said gene.
Group II, claim(s) 7-14, 17, 18, 20 and 23, drawn to a second product, an isolated double domain mutant AL2 gene, and a second method, for preparing a transgenic plant transformed with said gene.

The inventions listed as Groups I & II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The double domain mutants of Group II are not shared with the method of Group I. The method of increasing virus susceptibility of Group I is not shared with the method of Group II.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

   ☐ all parts.

   ☐ the parts relating to claims Nos. .

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/12680

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-23	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-23	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-23	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-23 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest isolated single or double domain mutants of a geminivirus AL2 transcription activator protein, nor methods to use the single domain mutant to create plants that are more susceptible to viral infection. The claims have industrial applicability in that the mutant nucleic acid sequences may be used to study transcription factor interaction, plant defense repsonses, and viral pathogenesis.

---------- NEW CITATIONS ----------

NONE

VII. Certain d fects in the international application

The following defects in the form or contents of the international application have been noted:

Claims 20-23 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: Each of claims 20-23 are missing the period punctuation mark.

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof: The amino acid and nucleotide sequences that appear in Figures 1 and 2 should be identified by their SEQ ID NOs.

Page 16, lines 19-20 indicates that transgenic plants were made comprising mutant AL2 genes shown in Table III. However, the description does not include a Table III.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-23 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not adequately described in writing, as required under PCT Rule 5.1(a)(iii), for the reasons set forth in the following paragraph.

The claims are broadly drawn to any isolated single domain recombinant AL2 gene encoding a modified transcription activator protein, comprising a mutation in the region which encodes from about amino acid 83 to amino acid 129 of the corresponding wild-type transcription activator protein; any isolated double domain recombinant AL2 gene, comprising a mutation in the region encoding from about amino acid 83 to about amino acid 129, and in the region encoding from about amino acid 23 to about amino acid 43, of the encoded transcriptional activator protein; any vector containing said single or double domain genes; a method of preparing a plant that is more susceptible to Begomoviruses or Curtoviruses; and a method of preparing transgenic plants containing said gene.

The description only states that single domain AL2 mutant genes with C-terminal truncations or alanine substitutions were made. The description also only states that double domain mutant AL2 genes contain either a combination of cysteine substitutions, particularly at positions 33, 35, and 43, or a histidine to alanine substitution at position 40 of the encoded protein, and a mutation in the 3' region of the gene. All mutations are in regards to only the TGMV AL2 gene. The description does not describe the nucleotide sequences of any of the claimed isolated double domain mutant recombinant AL2 genes. No details of the PCR site-directed mutagenesis reactions conducted to make the double domain mutants, including the PCR primer sequences, are described. The claimed mutant genes are therefore not reduced to practice. A gene is not reduced to practice until the inventor can define it by its physical or chemical properties,e.g. a DNA sequence. The disclosure of a few gene sequences do not enable claims broadly drawn to any analog thereof. Given the breadth of the claims, and the lack of guidance as discussed above, the description fails to provide an adequate written description of all of the single and double domain mutant AL2 genes encompassed by the claims.

Claims 1-23 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

The claims are broadly drawn to any isolated single domain recombinant AL2 gene encoding a modified transcription activator protein, comprising a mutation in the region which encodes from about amino acid 83 to amino acid 129 of the corresponding wild-(Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/00, 15/33, 15/63, 15/82, 15/90; AO1H 5/00 and US Cl.: 435/69.1, 320.1, 468; 536/23/72; 800/278, 279, 288, 295, 298, 301

I. BASIS OF REPORT:

5. (Some) amendments are considered to go beyond the disclosure as filed:
NONE

VIII. CERTAIN OBSERVATIONS ON THE APPLICATION (Continued):
type transcription activator protein; any isolated double domain recombinant AL2 gene, comprising a mutation in the region encoding from about amino acid 83 to about amino acid 129, and in the region encoding from about amino acid 23 to about amino acid 43, of the encoded transcriptional activator protein; any vector containing said single or double domain genes; a method of preparing a plant that is more susceptible to Begomoviruses or Curtoviruses; and a method of preparing transgenic plants containing said gene.

The description only states that single domain AL2 mutant genes with C-terminal truncations or alanine substitutions were made, and that double domain mutant AL2 genes contain either a combination of cysteine substitutions, particularly at positions 33, 35, and 43, or a histidine to alanine substitution at position 40 of the encoded protein, and a mutation in the 3' region of the gene. These mutations are in regards to only the TGMV AL2 gene. No details of any of the PCR site-directed mutagenesis reactions, which were conducted to make these double domain mutants, are provided. Some details of the construction of single domain mutants are provided. However, except for the cysteine and histidine residue substitutions with alanine, it is not specified if any of the single domain mutations were used in the construction of the double domain mutants, and if so, which ones and how they were combined. Concerning the claimed second mutation, no deletion of the central region of the AL2 gene was made. Therefore, one skilled in the art would not know what nucleotide sequences to remove.

Further, the description states that the mutant genes coding for single amino acid substitutions of alanine in place of either cysteine 33 or 43 still interacted with SNF-1 kinase. No effect of the C35A substitution is given. Therefore, it is unpredictable what the effect of the plurality of cysteine substitutions would confer on the encoded protein activity. Further, Sunter et al (1997) teach that the AL2 protein induces coat protein gene expression by different, and unknown, mechanisms in different cells types (pages 274-276). The domains and sequences of AL2 that are essential to these different mechanisms were unknown at the time the invention was made. It is therefore unpredictable how these mechanisms would be affected by the claimed mutant genes. Further, concerning the amino acid substitutions, only alanine was used to replace a native amino acid. As the mechanism of action of the AL2 protein is unknown, one cannot predict the effect of using any of the other claimed amino acids for the substitution mutations. The description states that the double domain mutants are useful for producing transgenic plants that are more resistant to infection by geminiviruses. The single domain mutants increase the susceptibility to virus when expressed in transgenic plants. It is unpredictable if any double domain mutant would confer virus resistance without experimentation. The double domain mutants were not tested for any activity or effect of any kind. It would require undue experimentation to test the double domain mutants for an effect on any of these activities. Given the claim breadth encompassing any type of single and double domain mutations of any AL2 gene, unpredictability of the art and lack of guidance as discussed, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim 21 and 22 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

The claims are broadly drawn towards a method for preparing a plant that is more susceptible to infection by Begomoviruses or Curtoviruses, comprising transforming a Begomovirus- or Curtovirus-host plant with any single domain mutant of an AL2 gene.

The description enables the production of transgenic plants harboring the disclosed single domain mutant AL2 genes that are more susceptible to the TGMV and BCTV Begomiviruses. However, it does not demonstrate that the transgenic plants had increased susceptibility to Curtoviruses. AL2 genes are not present within all geminiviruses. They are present in Begomovirus subgroup of geminivirus, and have been documented to be interchangeable between different Begomoviruses (Hartitz et al, page 1). However, AL2 genes have not been shown to be within Curtoviruses, or to complement mutant Curtoviruses. It is therefore unpredictable whether the disclosed transgenic plants harboring single domain AL2 genes would be more susceptible to any virus other than Begomoviruses. The description, not the knowledge of one skilled in the art, must enable the claimed invention. Given the breadth of the claims encompassing increased susceptibility to Curtoviruses,

Supplem ntal Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: B xes I - VIII

unpredictability of the art and lack of guidance of the description as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claims 1-5 and 7-23 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): The recitations "about amino acid 83 to about amino acid 129" in claims 1 and 7, "about amino acid 115 to amino acid 129" in claims 2 and 8, and "about amino acid 23 to about amino acid 43" in claim 7 render the claims indefinite. It is unknown what is meant by "about". For example in claim 1, is amino acid 75 encompassed? The metes and bounds of the claims, and the claims dependent thereon, are not clear.

Further regarding claim 11- the claim refers back to "said mutation" of claim 7. Claim 7 describes two mutations. It is unknown which mutation "said mutation" is referring to.

Further regarding claims 10 and 11- the claims are "Markush"-type claims that employ improper Markush terminology. Examples of proper Markush terminology, for a hypothetical claim in which an item from a group consisting of A, B, C, and D, is to be chosen, are 1) the chosen item is A, B, C, or D; 2) the chosen item is selected from the group consisting of A, B, C, and D. The claims appear to be missing the recitation "group consisting of".

16

PATENT COOPERATION TREATY

PCT

REC'D 10 AUG 2000

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rul 70)

Applicant's or agent's file reference 22727/04039	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US99/12680	International filing date *(day/month/year)* 04 JUNE 1999	Priority date *(day/month/year)* 05 JUNE 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant THE OHIO STATE RESEARCH FOUNDATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☒ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☒ Certain defects in the international application

   VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30 DECEMBER 1999	28 JULY 2000
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ASHWIN MEHTA Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/12680

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-21 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 22-24 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-5 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [X] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/12680

III. Non-establishment of pini n with regard t novelty, inventiv step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 24

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 24.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/12680

IV. Lack f unity f inventi n

1. In response to the invitation t restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s)1-6, 15, 16, 19, 21 and 22, drawn to a first product, an isolated single domain AL2 gene, and a first method for preparing a plant that is more susceptible to viral infection, comprising transforming a plant sample with said gene.
Group II, claim(s) 7-14, 17, 18, 20 and 23, drawn to a second product, an isolated double domain mutant AL2 gene, and a second method, for preparing a transgenic plant transformed with said gene.

The inventions listed as Groups I & II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The double domain mutants of Group II are not shared with the method of Group I. The method of increasing virus susceptibility of Group I is not shared with the method of Group II.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☐ the parts relating to claims Nos. _.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/12680

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supp rting such statement

1. statement

Novelty (N)	Claims	1-23	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-23	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-23	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-23 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest isolated single or double domain mutants of a geminivirus AL2 transcription activator protein, nor methods to use the single domain mutant to create plants that are more susceptible to viral infection. The claims have industrial applicability in that the mutant nucleic acid sequences may be used to study transcription factor interaction, plant defense repsonses, and viral pathogenesis.

---------- NEW CITATIONS ----------

NONE

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claims 20-23 are objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: Each of claims 20-23 are missing the period punctuation mark.

The description is objected to as containing the following defect(s) under PCT Rule 66.2(a)(iii) in the form or contents thereof: The amino acid and nucleotide sequences that appear in Figures 1 and 2 should be identified by their SEQ ID NOs.

Page 16, lines 19-20 indicates that transgenic plants were made comprising mutant AL2 genes shown in Table III. However, the description does not include a Table III.

VIII. Certain observati ns n the international application

The following bservations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-23 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not adequately described in writing, as required under PCT Rule 5.1(a)(iii), for the reasons set forth in the following paragraph.

The claims are broadly drawn to any isolated single domain recombinant AL2 gene encoding a modified transcription activator protein, comprising a mutation in the region which encodes from about amino acid 83 to amino acid 129 of the corresponding wild-type transcription activator protein; any isolated double domain recombinant AL2 gene, comprising a mutation in the region encoding from about amino acid 83 to about amino acid 129, and in the region encoding from about amino acid 23 to about amino acid 43, of the encoded transcriptional activator protein; any vector containing said single or double domain genes; a method of preparing a plant that is more susceptible to Begomoviruses or Curtoviruses; and a method of preparing transgenic plants containing said gene.

The description only states that single domain AL2 mutant genes with C-terminal truncations or alanine substitutions were made. The description also only states that double domain mutant AL2 genes contain either a combination of cysteine substitutions, particularly at positions 33, 35, and 43, or a histidine to alanine substitution at position 40 of the encoded protein, and a mutation in the 3' region of the gene. All mutations are in regards to only the TGMV AL2 gene. The description does not describe the nucleotide sequences of any of the claimed isolated double domain mutant recombinant AL2 genes. No details of the PCR site-directed mutagenesis reactions conducted to make the double domain mutants, including the PCR primer sequences, are described. The claimed mutant genes are therefore not reduced to practice. A gene is not reduced to practice until the inventor can define it by its physical or chemical properties,e.g. a DNA sequence. The disclosure of a few gene sequences do not enable claims broadly drawn to any analog thereof. Given the breadth of the claims, and the lack of guidance as discussed above, the description fails to provide an adequate written description of all of the single and double domain mutant AL2 genes encompassed by the claims.

Claims 1-23 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

The claims are broadly drawn to any isolated single domain recombinant AL2 gene encoding a modified transcription activator protein, comprising a mutation in the region which encodes from about amino acid 83 to amino acid 129 of the corresponding wild-(Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation f: B xes I - VIII Sheet 10

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/00, 15/33, 15/63, 15/82, 15/90; AO1H 5/00 and US Cl.: 435/69.1, 320.1, 468; 536/23/72; 800/278, 279, 288, 295, 298, 301

I. BASIS OF REPORT:

5. (Some) amendments are considered to go beyond the disclosure as filed:
NONE

VIII. CERTAIN OBSERVATIONS ON THE APPLICATION (Continued):
type transcription activator protein; any isolated double domain recombinant AL2 gene, comprising a mutation in the region encoding from about amino acid 83 to about amino acid 129, and in the region encoding from about amino acid 23 to about amino acid 43, of the encoded transcriptional activator protein; any vector containing said single or double domain genes; a method of preparing a plant that is more susceptible to Begomoviruses or Curtoviruses; and a method of preparing transgenic plants containing said gene.

The description only states that single domain AL2 mutant genes with C-terminal truncations or alanine substitutions were made, and that double domain mutant AL2 genes contain either a combination of cysteine substitutions, particularly at positions 33, 35, and 43, or a histidine to alanine substitution at position 40 of the encoded protein, and a mutation in the 3' region of the gene. These mutations are in regards to only the TGMV AL2 gene. No details of any of the PCR site-directed mutagenesis reactions, which were conducted to make these double domain mutants, are provided. Some details of the construction of single domain mutants are provided. However, except for the cysteine and histidine residue substitutions with alanine, it is not specified if any of the single domain mutations were used in the construction of the double domain mutants, and if so, which ones and how they were combined. Concerning the claimed second mutation, no deletion of the central region of the AL2 gene was made. Therefore, one skilled in the art would not know what nucleotide sequences to remove.

Further, the description states that the mutant genes coding for single amino acid substitutions of alanine in place of either cysteine 33 or 43 still interacted with SNF-1 kinase. No effect of the C35A substitution is given. Therefore, it is unpredictable what the effect of the plurality of cysteine substitutions would confer on the encoded protein activity. Further, Sunter et al (1997) teach that the AL2 protein induces coat protein gene expression by different, and unknown, mechanisms in different cells types (pages 274-276). The domains and sequences of AL2 that are essential to these different mechanisms were unknown at the time the invention was made. It is therefore unpredictable how these mechanisms would be affected by the claimed mutant genes. Further, concerning the amino acid substitutions, only alanine was used to replace a native amino acid. As the mechanism of action of the AL2 protein is unknown, one cannot predict the effect of using any of the other claimed amino acids for the substitution mutations. The description states that the double domain mutants are useful for producing transgenic plants that are more resistant to infection by geminiviruses. The single domain mutants increase the susceptibility to virus when expressed in transgenic plants. It is unpredictable if any double domain mutant would confer virus resistance without experimentation. The double domain mutants were not tested for any activity or effect of any kind. It would require undue experimentation to test the double domain mutants for an effect on any of these activities. Given the claim breadth encompassing any type of single and double domain mutations of any AL2 gene, unpredictability of the art and lack of guidance as discussed, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim 21 and 22 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

The claims are broadly drawn towards a method for preparing a plant that is more susceptible to infection by Begomoviruses or Curtoviruses, comprising transforming a Begomovirus- or Curtovirus-host plant with any single domain mutant of an AL2 gene.

The description enables the production of transgenic plants harboring the disclosed single domain mutant AL2 genes that are more susceptible to the TGMV and BCTV Begomiviruses. However, it does not demonstrate that the transgenic plants had increased susceptibility to Curtoviruses. AL2 genes are not present within all geminiviruses. They are present in Begomovirus subgroup of geminivirus, and have been documented to be interchangeable between different Begomoviruses (Hartitz et al, page 1). However, AL2 genes have not been shown to be within Curtoviruses, or to complement mutant Curtoviruses. It is therefore unpredictable whether the disclosed transgenic plants harboring single domain AL2 genes would be more susceptible to any virus other than Begomoviruses. The description, not the knowledge of one skilled in the art, must enable the claimed invention. Given the breadth of the claims encompassing increased susceptibility to Curtoviruses,

Supplem ntal Box
(T be used wh n the space in any f the preceding boxes is not sufficient)

Continuati n f: B xes I - VIII

unpredictability of the art and lack of guidance of the description as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claims 1-5 and 7-23 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims are indefinite for the following reason(s): The recitations "about amino acid 83 to about amino acid 129" in claims 1 and 7, "about amino acid 115 to amino acid 129" in claims 2 and 8, and "about amino acid 23 to about amino acid 43" in claim 7 render the claims indefinite. It is unknown what is meant by "about". For example in claim 1, is amino acid 75 encompassed? The metes and bounds of the claims, and the claims dependent thereon, are not clear.

Further regarding claim 11- the claim refers back to "said mutation" of claim 7. Claim 7 describes two mutations. It is unknown which mutation "said mutation" is referring to.

Further regarding claims 10 and 11- the claims are "Markush"-type claims that employ improper Markush terminology. Examples of proper Markush terminology, for a hypothetical claim in which an item from a group consisting of A, B, C, and D, is to be chosen, are 1) the chosen item is A, B, C, or D; 2) the chosen item is selected from the group consisting of A, B, C, and D. The claims appear to be missing the recitation "group consisting of".

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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : C12N 15/00, 15/33, 15/63, 15/82, 15/90, A01H 5/00 | A3

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(71) Applicant *(for all designated States except US)*: THE OHIO STATE RESEARCH FOUNDATION [US/US]; 1960 Kenny Road, Columbus, OH 43210-1063 (US).

(72) Inventor; and

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(74) Agent: DOCHERTY, Pamela, A.; Calfee, Halter & Griswold LLP, 1400 McDonald Investment Center, 800 Superior Avenue, Cleveland, OH 44114 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report:
15 June 2000 (15.06.00)

(54) Title: MUTANT FORMS OF THE AL2 GENE OF GEMINIVIRUSES

(57) Abstract

Isolated double domain mutant AL2 genes of a geminivirus are provided. The double domain AL2 mutant gene comprises at least one mutation in the 3' region of the AL2 gene, i.e., the region which encodes about 30 amino acids extending from about amino acid 100 to about amino acid 129 of the wild-type AL2 gene product and at least one mutation in the central region of the AL2 gene, i.e., the region which encodes about 20 amino acids extending from about amino acid 23 to about amino acid 43 of the wild-type AL2 gene product. Isolated single domain mutant AL2 genes of a geminivirus are also provided. The single domain mutant AL2 gene comprises at least one mutation in the 3' region of the AL2 gene, the region which encodes about 30 amino acids extending from about amino acid 100 to about amino acid 129 of the wild-type AL2 gene product. The present invention also relates to vectors comprising a double domain mutant AL2 gene and to vectors comprising a single domain mutant AL2 gene. The present invention also relates to transgenic plants comprising a double domain mutant AL2 gene and to transgenic plants comprising a single domain mutant AL2 gene.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/12680

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/00, 15/33, 15/63, 15/82, 15/90; A01H 5/00
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.1, 320.1, 468; 536/23/72; 800/278, 279, 288, 295, 298, 301

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WEST, Agricola Caplus, Biosis

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A, P	GILLETTE et al. Genetic Determinants Of Host-Specificity In Bipartite Geminivirus DNA A Components. Virology. 1998, Vol. 251, pages 361-369, especially pages 363-364.	1-23
A	SUNG et al. Mutational Analysis Of Potato Yellow Mosaic Geminivirus. J. Gen. Virol. 1995, Vol. 76, pages 1773-1780, especially pages 1777-1778.	1-6, 15, 16, 19, 21, 22
Y	SUNTER et al. Regulation Of A Geminivirus Coat Protein Promoter By AL2 Protein (TraP): Evidence For Activation And Derepression Mechanisms. Virology. 1997, Vol. 232, pages 269-280, entire document.	1-23

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 10 MARCH 2000	Date of mailing of the international search report 19 APR 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer ASHWIN MEHTA JOYCE BRIDGERS PARALEGAL SPECIALIST CHEMICAL MATRIX Telephone No. (703) 308-0196

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/12680

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A,T,P	HARTITZ et al. The Tomato Golden Mosaic Virus Transactivator (TrAP) Is A Single-Stranded DNA and Zinc-Binding Phosphoprotein With An Acidic Activation Domain. Virology. 1999, Vol. 263, pages 1-14, see whole document.	1-23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/12680

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
1-23

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/12680

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

435/69.1, 320.1, 468; 536/23/72; 800/278, 279, 288, 295, 298, 301

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1-6, 15, 16, 19, 21 and 22, drawn to a first product, an isolated single domain AL2 gene, and a first method for preparing a plant that is more susceptible to viral infection, comprising transforming a plant sample with said gene.
Group II, claim(s)7-14, 17, 18, 20 and 23, drawn to a second product, an isolated double domain mutant AL2 gene, and a second method, for preparing a transgenic plant transformed with said gene.
Group III, claim(s) 24, drawn to a third product, an isolated nucleic acid encoding the transcription activation domain of the transcription activation protein of TGMV.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The double domain mutants of Group II are not share with the method of Group I. The method of increasing virus susceptibility of Group I is not shared with the method of Group II. The nucleic acid of Group III is not shared with the methods of Groups I and II, and can be chemically synthesized.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 22727/04039	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5
International application No. PCT/US99/12680	International filing date *(day/month/year)* 04 JUNE 1999	(Earliest) Priority Date *(day/month/year)* 05 JUNE 1998
Applicant THE OHIO STATE RESEARCH FOUNDATION		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (See Box II).

4. With regard to the **title**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/12680

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

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Please See Extra Sheet.

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WEST, Agricola Caplus, Biosis

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"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
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Group II, claim(s)7-14, 17, 18, 20 and 23, drawn to a second product, an isolated double domain mutant AL2 gene, and a second method, for preparing a transgenic plant transformed with said gene.
Group III, claim(s) 24 drawn to a third product, an isolated nucleic acid encoding the transcription activation domain of the transcription activation protein of TGMV.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The double domain mutants of Group II are not share with the method of Group I. The method of increasing virus susceptibility of Group I is not shared with the method of Group II. The nucleic acid of Group III is not shared with the methods of Groups I and II, and can be chemically synthesized.